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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/755,701	01/05/2001	Allan S. Hoffman	UWOTL119001	3998

26389 7590 11/09/2004

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EXAMINER	
TRAN, MY CHAU T	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 11/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/755,701	HOFFMAN ET AL.	
	Examiner	Art Unit	
	MY-CHAU T TRAN	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-4,6,8-10 and 13-36* is/are pending in the application.

4a) Of the above claim(s) *18 and 20-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-4, 6, 8-10,13-17,19 and 33-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/24/03 & 8/12/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Applicant's response filed 8/16/2004 is acknowledged and entered.

2. Claims 11, and 37 were canceled and Claims 3, 8, and 13 were amended by the supplemental amendment filed on 2/18/2004.

3. Claims 1, 5, 7, and 12 were canceled; Claims 2-4, 6, 8-11, and 13-19 were amended; and Claims 33-37 were added by the amendment filed on 6/24/2003.

4. Claims 2-4, 6, 8-10, 13-36 are pending.

Election/Restrictions

5. Applicant has elected with traverse the following species for the elected invention (Claims 2-4, 6, 8-10, 13-36) in the reply filed on 5/10/2004 and 8/16/2004:

a. A ***single specific*** species of hydrophobic component. Applicant has elected the terpolymer of dimethylaminoethyl methacrylate (DMAEMA), butyl methacrylate (BMA), and styrene benzaldehyde, which is described in Example 2 and illustrated in Figures 4 and 5.

b. A ***single specific*** species of hydrophilic component. Applicant has elected polyalkylene oxide (e.g., PEG).

c. A ***single specific*** species of pH-sensitive linkage. Applicant has elected acetal.

d. A ***single specific*** species of agent that is to be transported through the membrane. Applicant has elected therapeutic agents (e.g., oligonucleotides). However, this species election is withdrawn in view of applicant's argument (see paragraph 6).

e. A ***single specific*** species of ligand. Applicant has elected antibody (e.g., IgG). However, this species election is withdrawn in view of applicant's argument (see paragraph 6).

f. A ***single specific*** species of a pharmaceutically acceptable carrier. Applicant has elected microparticles. However, this species election is withdrawn in view of applicant's argument (see paragraph 6).

6. Applicant's election with traverse the species election (see above) in the reply filed on 5/10/2004 is acknowledged. The traversal is on the ground that the election of species regarding the species of agent, ligand, and carrier is not required for purposes of search and examination. This is found persuasive and the election of species regarding the species of agent, ligand, and carrier is withdrawn. Thus the species election requirements for the type of agent, ligand, and microparticles are withdrawn.

7. Claim 18 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to ***nonelected species***, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 5/10/2004 and 8/16/2004.

8. Claims 20-32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to ***nonelected inventions***, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 4/26/2004.

9. Applicant's attention is hereby directed to the following is a recitation of M.P.E.P. §821.04 regarding the restriction of claims to a product and processes of using the product, Rejoinder:

> Where product and process claims drawn to independent and distinct inventions are presented in the same application, applicant may be called upon under 35 U.S.C. 121 to elect claims to either the product or process. See MPEP § 806.05(f) and § 806.05(h). The claims to the nonelected invention will be withdrawn from further consideration under 37 CFR 1.142. See MPEP § 809.02(c) and § 821 through § 821.03. However, if applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product claim will be rejoined.
>
> Where product and process claims are presented in a single application and that application qualifies under the transitional restriction practice pursuant to 37 CFR 1.129(b), applicant may either (1) elect the invention to be searched and examined and pay the fee set forth in 37 CFR 1.17(s) and have the additional inventions searched and examined under 37 CFR 1.129(b)(2), or (2) elect the invention to be searched and examined and not pay the additional fee (37 CFR 1.129(b)(3)). Where no additional fee is paid, if the elected invention is directed to the product and the claims directed to the product are subsequently found patentable, process claims which either depend from or include all the limitations of the allowable product will be rejoined. If applicant chooses to pay the fees to have the additional inventions searched and examined pursuant to 37 CFR 1.129(b)(2), even if the product is found allowable, applicant would not be entitled to a refund of the fees paid under 37 CFR 1.129(b) by arguing that the process claims could have been rejoined. 37 CFR 1.26 states that "[m]oney paid by actual mistake or in excess will be refunded, but a mere change of purpose after the payment of money...will not entitle a party to demand such a return..." The fees paid under 37 CFR 1.129(b) were not paid by actual mistake nor paid in excess, therefore, applicant would not be entitled to a refund.
>
> In the event of rejoinder, the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104 - 1.106. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. If the application containing the rejoined claims is not in condition for allowance, the subsequent Office action may be made final, or, if the application was already under final rejection, the next Office action may be an advisory action.

The following is a recitation from paragraph five, "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. §103(b)" (1184 TMOG 86(March 26, 1996)):

> "However, in the case of an elected product claim, rejoinder will be permitted when a product claim is found allowable and the withdrawn process claim **depends from or otherwise includes all the limitations of** an allowed product claim. Withdrawn process claims not commensurate in scope with an allowed product claim will not be rejoined." (emphasis added)

In accordance with M.P.E.P. §821.04 and *In re* Ochiai, 71 F.3d 1565, 37 USPQ 1127 (Fed. Cir. 1995), rejoinder of product claims with process claims commensurate in scope with the allowed product claims will occur following a finding that the product claims are allowable. Until, such time, a restriction between product claims and process claims is deemed proper. Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution to maintain either dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

10. It is note that applicant has amended the product claims, i.e. amendment filed on 6/24/2003 and 2/18/2004, and did not also amended the process claims. Thus applicant has loss the right to the rejoinder of the process claims with the product claimed in the event that the product claims is found allowable. (See M.P.E.P. §821.04 and *In re* Ochiai, 71 F.3d 1565, 37 USPQ 1127 (Fed. Cir. 1995)). Additionally, applicant was advised of the right to rejoinder and its condition for the rejoinder with regard to the product claims and process claims in the Office Action mailed 7/16/2002.

Priority

11. This application claims priority to a provisional application 60/174,893 filed 1/7/2000.

12. Claims 2-4, 6, 8-10, 13-17, 19, and 33-36 are treated on the merit in this Office Action.

Withdrawn Rejections

13. The rejection(s) of claims 1-19 under 35 USC 112, first paragraph, has been withdrawn in light of applicant's amendments of claims 2-4, 6, 8-11, and 13-19, addition of claims 33-37, and cancellation of claims 1, 5, 7, 11-12, and 37.

14. The rejections of claims 1-19 under 35 USC 112, second paragraph, have been withdrawn in light of applicant's amendments of claims 2-4, 6, 8-11, and 13-19, addition of claims 33-37, and cancellation of claims 1, 5, 7, 11-12, and 37.

15. The rejection of claims 1-19 under 35 USC 103(a) as being obvious over Choi et al. (US Patent 6,210,717 B1) has been withdrawn in view of applicant's cancellation of claim 1, and the new ground(s) of rejection.

16. The rejection of claims 1-19 under 35 USC 103(a) as being obvious over Heller et al. (US Patent 5,939,453) has been withdrawn in view of applicant's cancellation of claim 1, and the new ground(s) of rejection.

New Rejections – Necessitated by Amendment

Claim Rejections - 35 USC § 112

17. Claims 2-4, 6, 8, 13, 16-17, and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) The limitation of "*wherein the hydrophilic component is at least one of a hydrophilic group, a hydrophilic polymer, or a hydrophilic therapeutic, diagnostic, or prophylactic agent*" of claim 2 is an improperly written Markush language. The phrase 'at least one of' is vague because it is unclear if it is referring to the 'type' of hydrophilic component or the "number" of a hydrophilic group, a hydrophilic polymer, a hydrophilic therapeutic agent, a diagnostic agent, or a prophylactic agent in the hydrophilic component. It is suggested that for clarity the limitation be rewritten as "wherein the hydrophilic component is", which is a properly written Markush.

b) The limitation of "*wherein the therapeutic, diagnostic, or prophylactic agent is at least one of a protein, peptide, nucleotide, saccharide, polysaccharide, organic molecule, or combination thereof*" of claim 3 is an improperly written Markush language. The phrase 'at least one of' is vague because it is unclear if it is referring to the 'type' of agent or the "number" of a protein, peptide, nucleotide, saccharide, polysaccharide, organic molecule, or combination thereof in the agent. It is suggested that for clarity the limitation be rewritten as "wherein the agent is a protein, peptide, nucleotide, saccharide, polysaccharide, organic molecule, or combination thereof", which is a properly written Markush.

c) The limitation of "*wherein the hydrophobic component is at least one of a synthetic vinyl-type hydrophobic polymer, a non-vinyl-type hydrophobic polymer, naturally derived*

polymer, a membrane disruptive peptide, or a phospholipids bilayer disrupting agent" of claim 4 is an improperly written Markush language. The phrase 'at least one of' is vague because it is unclear if it is referring to the 'type' of hydrophobic component or the "number" of a synthetic vinyl-type hydrophobic polymer, a non-vinyl-type hydrophobic polymer, naturally derived polymer, a membrane disruptive peptide, or a phospholipids bilayer disrupting agent in the hydrophobic component. It is suggested that for clarity the limitation be rewritten as "wherein the hydrophobic component is a synthetic vinyl-type hydrophobic polymer, a non-vinyl-type hydrophobic polymer, naturally derived polymer, a membrane disruptive peptide, or a phospholipids bilayer disrupting agent", which is a properly written Markush.

d) The limitation of "*wherein the hydrophilic group is at least one of a hydroxyacid, amine, thiol, carboxyl group, amino acid, or small molecule comprising one of these groups*" of claim 6 is an improperly written Markush language. The phrase 'at least one of' is vague because it is unclear if it is referring to the 'type' of hydrophilic group or the "number" of a hydroxyacid, amine, thiol, carboxyl group, amino acid, or small molecule comprising one of these groups in the hydrophilic group. It is suggested that for clarity the limitation be rewritten as "wherein the hydrophilic group is a hydroxyacid, amine, thiol, carboxyl group, amino acid, or small molecule comprising one of these groups", which is a properly written Markush.

e) The limitation of "*wherein the pH-sensitive linkage is at least one of an acetal, orthoester, cis-aconityl group, carboxylic acid, hydrazone, phosphamide, ester, Schiff base, vinyl ether, dithioacetal, tert butyl ester, carbamate, urethane, anhydride, polysaccharide, amide, thiourea, urea, thioester, sulfonamide, phosphoramidate, or amine N-oxide*" of claim 8 is an improperly written Markush language. The phrase 'at least one of' is vague because it is unclear

if it is referring to the 'type' of pH-sensitive linkage or the "number" of an acetal, orthoester, cis-aconityl group, carboxylic acid, hydrazone, phosphamide, ester, Schiff base, vinyl ether, dithioacetal, tert butyl ester, carbamate, urethane, anhydride, polysaccharide, amide, thiourea, urea, thioester, sulfonamide, phosphoramidate, or amine N-oxide in the pH-sensitive linkage. It is suggested that for clarity the limitation be rewritten as "wherein the pH-sensitive linkage is an acetal, orthoester, cis-aconityl group, carboxylic acid, hydrazone, phosphamide, ester, Schiff base, vinyl ether, dithioacetal, tert butyl ester, carbamate, urethane, anhydride, polysaccharide, amide, thiourea, urea, thioester, sulfonamide, phosphoramidate, or amine N-oxide", which is a properly written Markush.

f) Claim 13 recites the limitation "conjugate" in line 2. There is insufficient antecedent basis for this limitation in the claim 33.

g) Claim 16 recites the limitation "conjugate" in line 2. There is insufficient antecedent basis for this limitation in the claim 33.

h) The limitation of "*wherein the carrier is at least one of a carrier for systemic, local, or topical delivery of the conjugate*" of claim 17 is an improperly written Markush language. The phrase 'at least one of' is vague because it is unclear if it is referring to the 'type' of carrier or the "number" of systemic, local, or topical delivery of the conjugate in the carrier. It is suggested that for clarity the limitation be rewritten as "wherein the carrier is systemic delivery of the conjugate, local delivery of the conjugate, or topical delivery of the conjugate".

i) The limitation of "*wherein the therapeutic, diagnostic, or prophylactic agent is at least one of an antisense nucleotide, ribozyme, ribozyme guide sequence, triplex forming oligonucleotide, or gene*" of claim 19 is an improperly written Markush language. The phrase

'at least one of' is vague because it is unclear if it is referring to the 'type' of agent or the "number" of nucleotide, ribozyme, ribozyme guide sequence, triplex forming oligonucleotide, or gene in the agent. It is suggested that for clarity the limitation be rewritten as "wherein the agent is nucleotide, ribozyme, ribozyme guide sequence, triplex forming oligonucleotide, or gene", which is a properly written Markush.

j) Claim 34 is vague and indefinite because it is an improperly written Markush language. It is unclear if the limitation of "further comprising a therapeutic, diagnostic, or prophylactic agent" refers to the 'type' of functionality in presently claimed composition or the additional 'structure' that is attached to the composition. It is suggested that for clarity the limitation be rewritten as "further comprising an agent wherein the agent is a therapeutic agent, a diagnostic agent, or a prophylactic agent", which is a properly written Markush.

Claim Rejections - 35 USC § 102

18. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an

international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

19. The presently claimed composition is interpreted as follows:

The instant claim 33 recites a composition. The composition comprises a hydrophilic conjugate. The hydrophilic conjugate have a hydrophobic component linked to a hydrophilic component by a pH-sensitive linkage, i.e. the linker.

The limitation that the pH-sensitive linkage is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5 to release the hydrophobic component is interpreted as a functional limitation of the linker. Additionally, the claimed pH-sensitive linkage would be interpreted as a bond between the hydrophobic component and the hydrophilic component because the type of pH-sensitive linkage claimed in claim 8 and supported by the specification disclosure (see e.g. pg. 23, lines 3-10), i.e. the claimed pH-sensitive linkage are "functional" group of either hydrophobic component or the hydrophilic component that produces a bond.

The limitation that the hydrophobic component is membrane-disruptive is a functional limitation of the hydrophobic component and allows enhanced transport through a cellular membrane is interpreted as a functional limitation of the hydrophobic component. Additionally, the limitation that the hydrophobic component is release from the hydrophilic conjugate is not a property of the claimed composition since the claimed composition comprises hydrophobic component and the hydrophilic component that are linked by a linkage. Thus this limitation is an improper limitation of the claimed composition.

20. Claims 2-4, 8-10, 14-15, and 33-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Kopecek et al. (US Patent 5,258,453).

Kopecek et al. disclose a drug delivery system (refers to the claimed composition) for the treatment of neo-plastic diseases (see e.g. Abstract; col. 1, lines 7-50; col. 3, lines 30-39; col. 6, lines 12-25; col. 10, lines 42-51). The system comprises a copolymer (refers to the claimed

hydrophobic component), a degradable drug carrier linkage (refers to the claimed pH-sensitive linkage), which is resistant to extracellular hydrolysis and it is subjected to controlled lyposomal hydrolysis (refers to the claimed hydrophilic component), and a target moiety (refers to the claimed agent) (see e.g. col. 3, lines 30-39; col. 6, lines 12-25; col. 10, lines 42-51). The drug carrier linkage comprises structure such as peptide spacer or linkage (see e.g. col. 3, line 59 to col. 4, line 9; col. 9, lines 3-33; col. 9, line 68 to col. 10, line 12; col. 11 to col. 16). The drug carrier linkage comprises and amine group that form an amide bond with the aldehyde group of copolymer, i.e. an amide linkage (see e.g. col. 11 to col. 16), and the drug carrier linkage is also attached to the anticancer drug via a peptide linkage (see e.g. col. 9, lines 34-36). The copolymer includes synthetic copolymer (see e.g. col. 8, lines 34-66). Thus, the composition of Kopecek et al. anticipates the presently claimed composition.

Additionally, the limitation that the pH-sensitive linkage is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5 to release the hydrophobic component is a functional limitation or a property of the claimed pH-sensitive linkage and it is presumed to be inherent. See MPEP § 2112.01. MPEP § 2112.01 states that:

> *II. >< COMPOSITION CLAIMS — IF THE COMPOSITION IS PHYSICALLY THE SAME, IT MUST HAVE THE SAME PROPERTIES*
>
> *"Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990) (Applicant argued that the claimed composition was a pressure sensitive adhesive containing a tacky polymer while the product of the reference was hard and abrasion resistant. "The Board correctly found that the virtual identity of monomers and procedures sufficed to support a prima facie case of unpatentability of Spada's polymer latexes for lack of novelty.").*

The peptide linkage, i.e. an amide linkage of Kopecek et al. is the same as the claimed pH-sensitive linkage of claim 8, i.e. amide. Thus, the claimed functional limitation of the pH-sensitive linkage is inherent to the peptide linkage Kopecek et al. The limitation that the hydrophobic component is membrane-disruptive and allows enhanced transport through a cellular membrane are a functional limitation or a property of the claimed hydrophobic conjugate and it is presumed to be inherent since the copolymer of Kopecek et al. is the same as the claimed hydrophobic component of claims 4 and 35.

21. Claims 2-4, 8-10, 14-15, and 33-35 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Kopecek et al. (US Patent 5,258,453).

Kopecek et al. disclose a drug delivery system (refers to the claimed composition) for the treatment of neo-plastic diseases (see e.g. Abstract; col. 1, lines 7-50; col. 3, lines 30-39; col. 6, lines 12-25; col. 10, lines 42-51). The system comprises a copolymer (refers to the claimed hydrophobic component), a degradable drug carrier linkage (refers to the claimed pH-sensitive linkage), which is resistant to extracellular hydrolysis and it is subjected to controlled lyposomal hydrolysis (refers to the claimed hydrophilic component), and a target moiety (refers to the claimed agent) (see e.g. col. 3, lines 30-39; col. 6, lines 12-25; col. 10, lines 42-51). The drug carrier linkage comprises structure such as peptide spacer or linkage (see e.g. col. 3, line 59 to col. 4, line 9; col. 9, lines 3-33; col. 9, line 68 to col. 10, line 12; col. 11 to col. 16). The drug carrier linkage comprises and amine group that form an amide bond with the aldehyde group of copolymer, i.e. an amide linkage (see e.g. col. 11 to col. 16), and the drug carrier linkage is also

attached to the anticancer drug via a peptide linkage (see e.g. col. 9, lines 34-36). The copolymer includes synthetic copolymer (see e.g. col. 8, lines 34-66). Thus, the composition of Kopecek et al. anticipates the presently claimed composition.

Alternatively, the claimed invention further differs from the prior art teachings only by the recitations of a) "*the pH-sensitive linkage is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5 to release the hydrophobic component*", i.e. the functional limitation of the pH-sensitive linkage, and b) "*the hydrophobic component is membrane-disruptive and allows enhanced transport through a cellular membrane only when released from the hydrophilic conjugate*", i.e. the functional limitation of the hydrophobic component. The claimed invention appears to be the same or obvious variations of the reference teachings, absent a showing of unobvious differences. The structural features of the composition of Kopecek et al. are the same as the structural features of the claimed composition, which are a hydrophobic component and a hydrophilic component that are linked by a pH-sensitive linkage. The office does not have the facilities and resources to provide the factual evidence needed in order to determine and/or compare the specific activities of the instant versus the reference pH-sensitive linkage and hydrophobic component wherein the ability of the pH-sensitive linkage is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5 to release the hydrophobic component and the ability of the hydrophobic component to be membrane-disruptive and allows enhanced transport through a cellular membrane only when released from the hydrophilic conjugate. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed array is different from the one taught by prior art and to establish the patentable differences. See *In re*

Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte* Gray 10 USPQ2d 1922(PTO Bd. Pat. App. & Int. 1989). See also MPEP 2112.01.

22. Claims 2-4, 8-10, 13-15, 19, and 33-36 are rejected under 35 U.S.C. 102(e) as being anticipated by Choi et al. (US Patent 6,210,717 B1).

Choi et al. discloses a composition for delivering a selected nucleic acid and various kinds of ligands into a targeted host cell (see e.g. Abstract; col. 2, lines 29-55; col. 3, lines 12-34; col. 3, lines 54-63). The composition is a copolymer transport molecule that is comprised of a hydrophilic portion, a hydrophobic portion, and a functional moiety (refers to the claimed agent) coupled to the hydrophilic portion (see e.g. col. 2, lines 29-55; col. 3, lines 12-26; col. 4, lines 60-62). The hydrophilic portion and hydrophobic portion are linked through as amide bond (refers to the claimed pH-sensitive linkage) (see e.g. col. 2, lines 29-55). The functional moiety includes ligand, and nucleic acid (see e.g. col. 3, lines 12-26). Thus the composition of Choi et al. anticipates the presently claimed composition.

Additionally, the limitation that the pH-sensitive linkage is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5 to release the hydrophobic component is a functional limitation or a property of the claimed pH-sensitive linkage and it is presumed to be inherent. See MPEP § 2112.01. MPEP § 2112.01 states that:

> *II. >< COMPOSITION CLAIMS — IF THE COMPOSITION IS PHYSICALLY THE SAME, IT MUST HAVE THE SAME PROPERTIES*
>
> *"Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990) (Applicant argued that the claimed composition was a pressure sensitive adhesive containing a tacky polymer while the product of the reference was hard and*

abrasion resistant. "The Board correctly found that the virtual identity of monomers and procedures sufficed to support a prima facie case of unpatentability of Spada's polymer latexes for lack of novelty.").

The amide bond of Choi et al. is the same as the claimed pH-sensitive linkage of claim 8, i.e. amide. Thus, the claimed functional limitation of the pH-sensitive linkage is inherent to the peptide linkage Choi et al. The limitation that the hydrophobic component is membrane-disruptive and allows enhanced transport through a cellular membrane are a functional limitation or a property of the claimed hydrophobic conjugate and it is presumed to be inherent since the copolymer of Choi et al. is the same as the claimed hydrophobic component of claims 4 and 35.

23. Claims 2-4, 8-10, 13-15, 19, and 33-36 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Choi et al. (US Patent 6,210,717 B1).

Choi et al. discloses a composition for delivering a selected nucleic acid and various kinds of ligands into a targeted host cell (see e.g. Abstract; col. 2, lines 29-55; col. 3, lines 12-34; col. 3, lines 54-63). The composition is a copolymer transport molecule that is comprised of a hydrophilic portion, a hydrophobic portion, and a functional moiety (refers to the claimed agent) coupled to the hydrophilic portion (see e.g. col. 2, lines 29-55; col. 3, lines 12-26; col. 4, lines 60-62). The hydrophilic portion and hydrophobic portion are linked through as amide bond (refers to the claimed pH-sensitive linkage) (see e.g. col. 2, lines 29-55). The functional moiety includes ligand, and nucleic acid (see e.g. col. 3, lines 12-26). Thus the composition of Choi et al. anticipates the presently claimed composition.

Alternatively, the claimed invention further differs from the prior art teachings only by the recitations of a) "*the pH-sensitive linkage is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5 to release the hydrophobic component*", i.e. the functional limitation of the pH-sensitive linkage, and b) "*the hydrophobic component is membrane-disruptive and allows enhanced transport through a cellular membrane only when released from the hydrophilic conjugate*", i.e. the functional limitation of the hydrophobic component. The claimed invention appears to be the same or obvious variations of the reference teachings, absent a showing of unobvious differences. The structural features of the composition of Choi et al. are the same as the structural features of the claimed composition, which are a hydrophobic component and a hydrophilic component that are linked by a pH-sensitive linkage. The office does not have the facilities and resources to provide the factual evidence needed in order to determine and/or compare the specific activities of the instant versus the reference pH-sensitive linkage and hydrophobic component wherein the ability of the pH-sensitive linkage is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5 to release the hydrophobic component and the ability of the hydrophobic component to be membrane-disruptive and allows enhanced transport through a cellular membrane only when released from the hydrophilic conjugate. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed array is different from the one taught by prior art and to establish the patentable differences. See *In re* Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte* Gray 10 USPQ2d 1922(PTO Bd. Pat. App. & Int. 1989). See also MPEP 2112.01.

24. Claims 2-4, 8-10, 13-16, 19, and 33-35 are rejected under 35 U.S.C. 102(e) as being anticipated by Heller et al. (US Patent 5,939,453).

Heller et al. discloses a composition that is block copolymers having both hydrophilic and hydrophobic blocks (see e.g. Abstract; col. 4, lines 1-11; col. 5, lines 10-17). This composition provides a pharmaceutical delivery system or for the sustained release of an active agent wherein the active agent include proteins and enzymes (see e.g. col. 4, lines 1-11, and 25-67). The hydrophilic block is PEG (polyethylene glycol) and the hydrophobic block is POE (poly(orthoester)), which is bioerodible (see e.g. col. 5, lines 10-17; col. 6, lines 7-35). The hydrophilic block is linked to the hydrophobic block via an acetal bond (refers to the pH-sensitive linkage) (see e.g. col. 8, lines 24-50; col. 8, line 63 to col. 9, line 15). The composition includes a pharmaceutical carrier (see e.g. col. 5, lines 58-67; col. 13, lines 47-60). Thus the composition of Heller et al. anticipates the presently claimed composition.

Additionally, the limitation that the pH-sensitive linkage is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5 to release the hydrophobic component is a functional limitation or a property of the claimed pH-sensitive linkage and it is presumed to be inherent. See MPEP § 2112.01. MPEP § 2112.01 states that:

> *II. >< COMPOSITION CLAIMS — IF THE COMPOSITION IS PHYSICALLY THE SAME, IT MUST HAVE THE SAME PROPERTIES*
>
> *"Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990) (Applicant argued that the claimed composition was a pressure sensitive adhesive containing a tacky polymer while the product of the reference was hard and abrasion resistant. "The Board correctly found that the virtual identity of monomers and procedures sufficed to support a prima facie case of unpatentability of Spada's polymer latexes for lack of novelty.").*

The acetal linkage of Heller et al. is the same as the claimed pH-sensitive linkage of claim 8, i.e. acetal. Thus, the claimed functional limitation of the pH-sensitive linkage is inherent to the peptide linkage Heller et al. The limitation that the hydrophobic component is membrane-disruptive and allows enhanced transport through a cellular membrane are a functional limitation or a property of the claimed hydrophobic conjugate and it is presumed to be inherent since the copolymer of Heller et al. is the same as the claimed hydrophobic component of claims 4 and 35.

25. Claims 2-4, 8-10, 13-16, 19, and 33-35 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Heller et al. (US Patent 5,939,453).

Heller et al. discloses a composition that is block copolymers having both hydrophilic and hydrophobic blocks (see e.g. Abstract; col. 4, lines 1-11; col. 5, lines 10-17). This composition provides a pharmaceutical delivery system or for the sustained release of an active agent wherein the active agent include proteins and enzymes (see e.g. col. 4, lines 1-11, and 25-67). The hydrophilic block is PEG (polyethylene glycol) and the hydrophobic block is POE (poly(orthoester)), which is bioerodible (see e.g. col. 5, lines 10-17; col. 6, lines 7-35). The hydrophilic block is linked to the hydrophobic block via an acetal bond (refers to the pH-sensitive linkage) (see e.g. col. 8, lines 24-50; col. 8, line 63 to col. 9, line 15). The composition includes a pharmaceutical carrier (see e.g. col. 5, lines 58-67; col. 13, lines 47-60). Thus the composition of Heller et al. anticipates the presently claimed composition.

Alternatively, the claimed invention further differs from the prior art teachings only by the recitations of a) "*the pH-sensitive linkage is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5 to release the hydrophobic component*", i.e. the functional limitation of the pH-sensitive linkage, and b) "*the hydrophobic component is membrane-disruptive and allows enhanced transport through a cellular membrane only when released from the hydrophilic conjugate*", i.e. the functional limitation of the hydrophobic component. The claimed invention appears to be the same or obvious variations of the reference teachings, absent a showing of unobvious differences. The structural features of the composition of Heller et al. are the same as the structural features of the claimed composition, which are a hydrophobic component and a hydrophilic component that are linked by a pH-sensitive linkage. The office does not have the facilities and resources to provide the factual evidence needed in order to determine and/or compare the specific activities of the instant versus the reference pH-sensitive linkage and hydrophobic component wherein the ability of the pH-sensitive linkage is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5 to release the hydrophobic component and the ability of the hydrophobic component to be membrane-disruptive and allows enhanced transport through a cellular membrane only when released from the hydrophilic conjugate. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed array is different from the one taught by prior art and to establish the patentable differences. See *In re* Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte* Gray 10 USPQ2d 1922(PTO Bd. Pat. App. & Int. 1989). See also MPEP 2112.01.

Conclusion

26. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MY-CHAU T TRAN whose telephone number is 571-272-0810. The examiner can normally be reached on Mon.: 8:00-2:30; Tues.-Thurs.: 7:30-5:00; Fri.: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANDREW WANG can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

mct
November 4, 2004

PADMASHRI PONNALURI
PRIMARY EXAMINER